CLAIMS

What is claimed as new and desired to be protected by Letters Patent of the United States is:

1. A label-free method for the classification of cellular events, wherein the classification is achieved through measuring changes in the electrical properties of cells after application of a stimulus the method comprising:
   (a) measuring a value of an electrical property for at least one frequency within a range of frequencies for each time point during a selected period of time for a cell with a receptor having a known receptor type and a known messenger pathway;
   (b) selecting a reference time point corresponding to a time period immediately prior to addition of a known stimulus;
   (c) adding a known stimulus;
   (d) calculating changes in the value of the electrical property for each frequency by subtracting the value of the measured electrical property for the reference time point from the value of the measured electrical property for each subsequent time point;
   (e) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;
   (f) and, comparing the parameterized changes in the value of the electrical property to parameter sets of known messenger pathways to assign the parameterized changes in value of the electrical property to a known stimulus/receptor interaction class.

2. The method of claim 1 wherein the cellular events are chosen from the group comprising signal transduction from ligand/receptor interactions, cytotoxicity, apoptosis, tumor cell progression, and stem cell differentiation.

3. The method of claim 1 wherein the electrical properties are chosen from the group comprising impedance phase, impedance

magnitude, complex reflection coefficients, total circuit resistance, and total circuit capacitance.

4. The method of claim 1 wherein the at least one frequency within a range of frequencies includes frequencies in the electromagnetic spectrum and acoustic frequencies.

5. The method of claim 1 wherein the range of frequencies is 40Hz to 110MHz.

6. The method of claim 1 wherein the stimulus is a substance.

7. The method of claim 6 wherein the substance is a small molecule ligand.

8. The method of claim 6 wherein the substance is a ligand, a protein, an antibody, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

9. The method of claim 1, wherein the classification is achieved in real time.

10. The method of claim 1 further comprising the steps of
(g) measuring the value of the electrical property for at least one frequency in a range of frequencies for each time point during a selected period of time for a cell with a known receptor type;
(h) selecting a reference time point corresponding to a time period immediately prior to addition of an unknown stimulus;
(i) adding the unknown stimulus;
(j) calculating changes in the value of the electrical property for each frequency by subtracting the value of the electrical property for the reference time point from the value of the electrical property for each subsequent time point after addition of the unknown stimulus;
(k) comparing the changes in the value of the electrical property after addition of the unknown stimulus to the changes in the value

of the electrical properties for known stimuli to correlate the changes in the value of the electrical property to a cellular response;

(l) and, assigning the cellular response to a known substance/receptor interaction class and classifying the stimulus.

11. The method of claim 1 further comprising the steps of

(g) measuring the value of the electrical property for at least one frequency within a range of frequencies for each time point during a selected period of time for a cell with an unknown receptor type;

(h) selecting a reference time point corresponding to a time period immediately prior to addition of a stimulus;

(i) adding the stimulus;

(j) calculating changes in the value of the electrical property for each frequency by subtracting the value of the electrical property for the reference time point from the value of the electrical property for each subsequent time point after addition of the stimulus;

(k) comparing the changes in the value of the electrical property after addition of the stimulus to the changes in the value of the electrical properties for known receptors to correlate the changes in the value of the electrical property to a cellular response;

(l) and, assigning the cellular response to a known substance/receptor interaction class and classifying the receptor.

12. A label-free method for the classification of cellular events, wherein the classification is achieved through measuring changes in the impedance of cells after application of a stimulus the method comprising:

(a) measuring the impedance over at least one frequency in a range of frequencies for each time point during a selected period of time for a cell with a known receptor type and a known messenger pathway;

(b) selecting a reference time point corresponding to a time period immediately prior to addition of a known stimulus;

(c) adding a known stimulus;

(d) calculating changes in impedance for each frequency by subtracting the impedance for the reference time point from the impedance for each subsequent time point;

(e) parameterizing the changes in impedance for each time point, receptor, and stimulus;

(f) and, comparing the parameterized changes in impedance to parameter sets of known messenger pathways to assign the parameterized changes in impedance to a known stimulus/receptor interaction class.

13. The method of claim 12 further comprising the steps of

(g) measuring the impedance over at least one frequency within a range of frequencies for each time point during a selected period of time for a cell with a known receptor type;

(h) selecting a reference time point corresponding to a time period immediately prior to addition of an unknown stimulus;

(i) adding the unknown stimulus;

(j) calculating changes in the impedance for each frequency by subtracting the value of the impedance for the reference time point from the value of the impedance for each subsequent time point after addition of the unknown stimulus;

(k) comparing the changes in the impedance after addition of the unknown stimulus to the changes in the impedance for known stimuli to correlate the changes in the impedance to a cellular response;

(l) and, assigning the cellular response to a known substance/receptor interaction class and classifying the stimulus.

14. The method of claim 12 further comprising the steps of

(g) measuring an impedance over at least one frequency within a range of frequencies for each time point during a selected period of time for a cell with an unknown receptor type;
(h) selecting a reference time point corresponding to a time period immediately prior to addition of a stimulus;
(i) adding the stimulus;
(j) calculating changes in impedance for each frequency by subtracting the impedance for the reference time point from the impedance for each subsequent time point after addition of the stimulus;
(k) comparing the changes in impedance after addition of the stimulus to the changes in impedance for known receptors to correlate the changes in impedance to a cellular response;
(l) and, assigning the cellular response to a known substance/receptor interaction class and classifying the receptor.

15. The method of claim 12 wherein the cellular events are chosen from the group comprising signal transduction from ligand/receptor interactions, cytotoxicity, apoptosis, tumor cell progression, and stem cell differentiation.

16. The method of claim 12 wherein the changes in impedance are measured as resistance or reactance.

17. The method of claim 12 wherein the changes in impedance are measured as admittance, conductance, or susceptance.

18. The method of claim 12 wherein the at least one frequency within a range of frequencies includes frequencies in the electromagnetic spectrum and acoustic frequencies.

19. The method of claim 12 wherein the range of frequencies is 40Hz to 110MHz.

20. The method of claim 12 wherein the stimulus is a substance.

21. The method of claim 20 wherein the substance is a small molecule ligand.

22. The method of claim 20 wherein the substance is a ligand, a protein, an antibody, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

23. The method of claim 12 wherein the classification is achieved in real-time.

24. A label-free method for the classification of cellular events, wherein the classification is achieved through measuring changes in the electrical properties of a circuit containing cells after application of a stimulus the method comprising:
(g) measuring a value of an electrical property for at least one frequency within a range of frequencies for each time point during a selected period of time for a circuit containing at least one cell,

the at least one cell of the circuit having a receptor with a known receptor type and a known messenger pathway;

(h) selecting a reference time point corresponding to a time period immediately prior to addition of a known stimulus;

(i) adding a known stimulus;

(j) calculating changes in the value of the electrical property for the circuit for each frequency by subtracting the value of the measured electrical property for the reference time point from the value of the measured electrical property for each subsequent time point;

(k) parameterizing the changes in the value of the electrical property for each time point, receptor, and stimulus;

(l) and, comparing the parameterized changes in the value of the electrical property to parameter sets of known messenger pathways to assign the parameterized changes in value of the electrical property to a known stimulus/receptor interaction class.

25. The method of claim 24 wherein the cellular events are chosen from the group comprising signal transduction from ligand/receptor interactions, cytotoxicity, apoptosis, tumor cell progression, and stem cell differentiation

26. The method of claim 24 wherein the electrical properties are chosen from the group comprising impedance phase, impedance magnitude, complex reflection coefficients, total circuit resistance, and total circuit capacitance.

27. The method of claim 24 wherein the at least one frequency within a range of frequencies includes frequencies in the electromagnetic spectrum and acoustic frequencies.

28. The method of claim 24 wherein the range of frequencies is 40Hz to 110MHz

29. The method of claim 24 wherein the stimulus is a substance.

30. The method of claim 29 wherein the substance is a small molecule ligand.

31. The method of claim 29 wherein the substance is a ligand, a protein, an antibody, a lipid, a carbohydrate, a nucleic acid, water, or an ion.

32. The method of claim 24, wherein the classification is achieved in real time.

33. The method of claim 24 further comprising the steps of
(m) measuring the value of the electrical property for at least one frequency in a range of frequencies for each time point during a selected period of time for a circuit containing at least one cell, the at least one cell of the circuit having a known receptor type;
(n) selecting a reference time point corresponding to a time period immediately prior to addition of an unknown stimulus;
(o) adding the unknown stimulus;
(p) calculating changes in the value of the electrical property for the circuit for each frequency by subtracting the value of the electrical property for the reference time point from the value of

the electrical property for each subsequent time point after addition of the unknown stimulus;

(q) comparing changes in the value of the electrical property after addition of the unknown stimulus to changes in the value of the electrical property for known stimuli to correlate changes in the value of the electrical property to a cellular response;

(r) and, assigning the cellular response to a known substance/receptor interaction class and classifying the stimulus.

34. The method of claim 24 further comprising the steps of

(m) measuring the value of the electrical property for at least one frequency within a range of frequencies for each time point during a selected period of time for a circuit containing at least one cell, the at least one cell having an unknown receptor type;

(n) selecting a reference time point corresponding to a time period immediately prior to addition of a stimulus;

(o) adding the stimulus;

(p) calculating changes in the value of the electrical property for each frequency by subtracting the value of the electrical property for the reference time point from the value of the electrical property for each subsequent time point after addition of the stimulus;

(q) comparing changes in the value of the electrical property after addition of the stimulus to changes in the value of the electrical property for known receptors to correlate changes in the value of the electrical property to a cellular response;

(r) and, assigning the cellular response to a known substance/receptor interaction class and classifying the receptor.

35. The method of claim 24 wherein the electrical circuit comprises interdigitated coplanar electrodes.